Remarks

The Amendments

Claim 1 has been amended to recite "[a] chemically modified double stranded nucleic acid molecule, wherein: the nucleic acid molecule comprises a separate sense strand and separate antisense strand, each having one or more pyrimidine nucleotides and one or more purine nucleotides; each strand of the nucleic acid molecule is 18 to 27 nucleotides in length; the antisense strand of the nucleic acid molecule comprises 18 to 27 nucleotides that are complementary to a GPRA RNA comprising SEQ ID NO: 811 the sense strand of the nucleic acid molecule is complementary to the antisense strand, and comprises a 18 to 27 nucleotide portion of the GPRA RNA sequence; about 50 to 100 percent of the nucleotides in each of the sense and antisense strands of the nucleic acid molecule are chemically modified with modifications independently selected from the group consisting of 2'-O-methyl, 2'-deoxy-2'-fluoro, 2'-deoxy, phosphorothioate and deoxyabasic modifications; and one or more of the purine nucleotides present in one or both strands of the nucleic acid molecule are 2'-O-methyl purine nucleotides and one or more of the pyrimidine nucleotides present in one or both strands of the nucleic acid molecule are 2'-deoxy-2'-fluoro pyrimidine nucleotides." Support for the amendment can be found in the specification at, *inter alia,* page 9, lines 16-27, page 13, lines 15-19, page 15, page 26, line 19 - page 27, line 25, page 151 (*see,* page NM_207173), and Figures 4-5, Tables III and IV, and throughout the specification. Support is also found in the priority documents. *See. e.g.,* U.S. patent application No: 10/923,182 (*see,* page 151 NM_207173) and U.S. Provisional patent application Nos. 60/363,124 (*see*, page 10, lines 3-20, page 12, lines 4-6, and 60/440,129 (*see,* page 7, lines 23-30, page 8, lines 5-11)

Claim 3 has been amended to recite "[t]he nucleic acid molecule of claim 1, wherein the nucleic acid molecule comprises one or more ribonucleotides." Support can be found within the specification at, *inter alia*, page 19, lines 3-5, and throughout the specification.

Claim 13 has been amended to recite "[t]he nucleic acid molecule of claim 1, wherein 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 or more of the pyrimidine nucleotides present in the sense strand are 2'-O-methyl pyrimidine nucleotides." Support can be found within the specification at, *inter alia*, page 36, lines 15-20 and throughout the specification. Support is also found in the priority documents. *See, e.g.,* U.S. Provisional patent application Nos. 60/363,124 (*see*, page 10, lines 3-16) and 60/440,129 (*see,* page 15, lines 14-20 and page 10, lines 10-13).

Claim 14 has been amended to recite "[t]he nucleic acid molecule of claim 1, wherein 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 or more of the purine nucleotides present in the sense strand are 2'-deoxy purine nucleotides." Support can be found within the specification at, *inter alia*, page 31, lines 22-28, and throughout the specification. Support is also found in the priority documents. *See, e.g.,* U.S. Provisional patent application No. 60/440,129 (*see,* page 22, lines 1-9 and page 10, lines 13-17).

Claim 15 has been amended to recite "[t]he nucleic acid molecule of claim 1, wherein 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 or more of the pyrimidine nucleotides present in the sense strand are 2'-deoxy-2'-fluoro pyrimidine nucleotides." Support can be found within the specification at, *inter alia*, page 36, lines 15-20, and throughout the specification. Support is also found in the priority documents. *See, e.g.,* U.S. Provisional patent application No. 60/363,124 (*see*, page 10, lines 3-16 and page 11, lines 1-11) and 60/440,129 (*see,* page 15, lines 14-20 and page 10, lines 10-13).

Claim 16 has been amended to recite "[t]he nucleic acid molecule of claim 1, wherein the sense strand includes a terminal cap moiety at the 5'-end, the 3'-end, or both the 5' and 3' ends of the sense strand." Support can be found within the specification at, *inter alia*, page 20, lines 24-31, page 38, lines 5-12 and throughout the specification. Support is also found in the priority documents. *See, e.g.,* U.S. Provisional patent application Nos. 60/363,124 (*see*, page 10, lines 3-16 and page 11, lines 1-11), and 60/440,129 (*see,* page 16, lines 19-25 and page 21).

Claim 17 has been amended to recite "[t]he nucleic acid molecule of claim 16, where in the terminal cap moiety is an inverted deoxy abasic moiety." Support can be found within the specification at, *inter alia*, page 20, lines 24-31, page 73, lines 11-17, and throughout the specification. Support is also found in the priority documents. *See, e.g.,* U.S. Provisional patent application No. 60/363,124 (*see*, page 40, lines 4-18) and 60/440,129 (*see,* page 20, lines 1-5).

Claim 18 has been amended to recite "[t]he nucleic acid molecule of claim 1, wherein 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 or more of the pyrimidine nucleotides present in the antisense strand are 2'-deoxy-2'-fluoro pyrimidine nucleotides." Support can be found within the specification at, *inter alia*, page 36, lines 15-20, and throughout the specification. Support is also found in the priority documents. *See, e.g.,* U.S. Provisional patent application No. 60/363,124 (*see*, page 10, lines 3-16 and page 11, lines 1-11) and 60/440,129 (*see,* page 15, lines 4-20 and page 10, lines 10-13).

Claim 19 has been amended to recite "[t]he nucleic acid molecule of claim 1, wherein 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 or more of the purine nucleotides present in the antisense strand are 2'-O-methyl purine nucleotides." Support can be found within the specification at, *inter alia*, page 47, lines 8-16,

and throughout the specification. Support is also found in the priority documents. *See, e.g.,* U.S. Provisional patent application No. 60/440,129 (*see,* page 22, lines 25-30 and page 10, lines 13-17).

Claim 20 has been amended to recite "[t]he nucleic acid molecule of claim 1, wherein 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 or more of the purine nucleotides present in the antisense strand are 2'-deoxy purine nucleotides. Support can be found within the specification at, *inter alia,* page 44, lines 1-9, and throughout the specification. Support is also found in the priority documents. *See, e.g.,* U.S. Provisional patent application No. 60/440,129 (*see,* page 23, lines 15-20 and page 10, lines 13-17).

Claim 21 has been amended to recite "[t]he nucleic acid molecule of claim 1, wherein the antisense strand comprises a terminal phosphorothioate internucleotide linkage at the 3'-end of the antisense strand." Support can be found within the specification at, *inter alia*, page 38, lines 13-16, page 31, lines 9-25, and throughout the specification. Support is also found in the priority documents. *See, e.g.,* U.S. Provisional patent application Nos. 60/363,124 (*see*, page 10, lines 31 - page 11, lines 1-11) and 60/440,129 (*see,* page 24, lines 13-18).

Claim 30 has been amended to recite "[t]he nucleic acid molecule of claim 1, wherein the antisense strand includes a terminal phosphate group." Support can be found within the specification at, *inter alia*, page 34, lines 18-27, and throughout the specification. Support is also found in the priority documents. *See, e.g.,* U.S. Provisional patent application No. 60/363,124 (*see*, page 9, lines 5-13) and 60/440,129 (*see,* page 13, lines 16-25).

Claim 31 has been amended to recite "[a] composition comprising the nucleic acid molecule of claim 1 in a pharmaceutically acceptable carrier or diluent." Support can be found within the specification at, *inter alia*, page 29, lines 16-17, and throughout the specification. Support is also found in the priority documents. *See, e.g.,* U.S. Provisional patent application Nos. 60/363,124 (*See*, page 18, lines 15-20).

New claim 36 recites "[t]he nucleic acid molecule of claim 19, wherein 1, 2, or 3 of the purine nucleotides present in the sense strand are 2'-O-methyl purine nucleotides." Support can be found within the specification at, *inter alia*, page 31, lines 22-28, and throughout the specification. Support is also found in the priority documents. *See, e.g.,* U.S. Provisional patent application No.60/440,129 (*see,* page 25, lines 20-25, page 10, lines 13-17).

New claim 37 recites "[a] method of inhibiting the expression of human GPRA comprising administering the nucleic acid molecule of claim 1 to a subject in need thereof that expresses human GPRA under conditions that allow for inhibition of human GPRA expression. Support can be found

within the specification at, *inter alia*, page 89, lines 5-7, page 90, lines 12-17, and throughout the specification.

Claims 2, 4-12, 22-29, and 32-35 have been canceled with this amendment without prejudice.

Amendments to the claims are made without prejudice and do not constitute amendments to overcome any prior art or other statutory rejections and are fully supported by the specification as filed. Additionally, these amendments are not an admission regarding the patentability of subject matter of the canceled or amended claims and should not be so construed. Applicant reserves the right to pursue the subject matter of the previously filed claims in this or in any other appropriate patent application. The amendments add no new matter and applicants respectfully request their entry.

Amendment to Specification

The specification has been amended in order to incorporate the sequence listing into the application. The amendment does not add new matter.

The Sequence Listing

Applicants have enclosed a revised sequence listing and request its entry in place of the previously entered sequence listing. Applicants have made the necessary request that it be incorporated into the specification. The sequence listing adds SEQ ID NO: 811. SEQ ID NO: 811 represents GenBank entry NM_207173. The version of NM_207173 appearing in the sequence listing as SEQ ID NO: 811 appeared in GenBank on April 15, 2004 and is included in the specification (*see e.g.,* page 151). The sequence listing adds no new matter and applicants respectfully request its entry.

The sequence listing is believed to comply fully with the sequence listing rules. Under EFS-Web filing procedures, Applicants believe that they need to submit only an electronic version of the sequence listing in order to comply with the pending Notice.

The Restriction Requirement

The Examiner asserts that a restriction is necessary for claim 33 because allegedly "the siNA compounds having SEQ ID NOs.: 1-806, which are targeted to a gene encoding a GPRA RNA does not comply with the requirements of unity of invention" and "the siNA sequences are considered to be each separate invention." Claim 33 has been canceled. As such, the restriction requirement is moot. Additionally, none of the remaining claims recite more than one sequence. Therefore, it is the Applicants' good faith belief that an election is not necessary.

Further, the Examiner asserts that a species election is necessary as between GenBank Accession No. NM_207173 or NM_207172 because they are "drawn to a different species of GPRA RNA." Applicants disagree. Nevertheless, in the interest of expediting prosecution, claim 32 has been canceled. As such, the species election is moot with respect to claim 8. Additionally, none of the remaining claims recite a GenBank Accession number for GPRA RNA. Therefore, it is in Applicants' good faith belief that a species election to a particular GenBank Accession No. is not necessary.

Conclusion

In view of the foregoing amendments and remarks, the applicant submits that the claims are in condition for allowance, which is respectfully solicited. If the examiner believes a teleconference will advance prosecution, she is encouraged to contact the undersigned as indicated below.

Respectfully submitted,

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Date: April 23, 2007

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